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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,706	12/11/2003	James E. Hagstrom	Mirus.048.01	8647

7590

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EXAMINER

KAUSHAL, SUMESH

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 01/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

10/733,706

Applicant(s)

HAGSTROM ET AL.

Examiner

Sumesh Kaushal Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

*Applicant's response filed on 12/11/03 has been acknowledged.*

*Claims 1-17 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.*

**Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Stedman et al (WO 99/31982, 1999).

The instant claims are drawn to a method for delivering polynucleotide to extra vascular parenchymal cell in a tissue of a mammal in-vivo by inserting a viral vector in the lumen of vessel, increasing vessel permeability within the tissue and delivering the viral vector out side the vessel.

Stedman teaches transvascular delivery of a composition comprising a viral vector to an extravascular tissue of a mammal. Regarding claims 1-4 the cited art teaches the transport of an adenovirus vector from the lumen of vascular capillaries to the interstitium of muscle tissue (page 53 example-1). Regarding claims 5-9 the cited art teaches delivery of a viral vector though an artery or a vein (example -1, pages 54-56). Regarding claims 11-12 the cited art teaches increasing vessel permeability by providing virus vector suspension continuously at high pressure (20 pounds per sq.

Art Unit: 1636

inch or 80 pounds per sq. inch) see page 55 lines 1-18. Regarding claims 11 the cited art further teaches increasing vascular permeability using permeability-enhancing agent is selected from the group consisting of histamine, acetylcholine, an adenosine nucleotide, arachidonic acid, bradykinin, cyanide, endothelin, endotoxin, interleukin-2, ionophore A23 187, nitroprusside, a leukotriene, an oxygen radical, phospholipase, platelet activating factor, protamine, serotonin, tumor necrosis factor, vascular endothelial growth factor, a venom, and a vasoactive amine (page 8, lines 18-28, page 20, page 63 example-2). Regarding claims 13 and 14 the cited art teaches the delivery of viral vector via increasing vascular permeability to muscle cells, cardiac muscle cell and liver cells (page 73 example-5, example-6, fig-4). Regarding claim 15-17 the cited art teaches increasing vessel permeability by providing virus vector suspension continuously at high pressure (20 pounds per sq. inch or 80 pounds per sq. inch) see page 55 lines 1-18). In addition the cited art further teaches increasing vascular permeability by occlusion of hepatic inflow (page 54 lines 21-28) and treatment with histamine prior to infusion of virus vector (page 55, line 25-28). Thus the cited art clearly anticipate the invention as claimed.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stedman et al (WO 99/31982, 1999) as applied to claims 1-9 and 11-17 above, and further in view of Wolf et al (US 6265387, 2001).

As stated above Stedman teaches transvascular delivery of a viral vector to an extravascular tissue of a mammal. Even though Stedman teaches the delivery of viral vectors via veins and arteries the cited art does not teaches the delivery of viral vectors through bile duct.

Wolf et al teaches a method for delivering polynucleotide sequences into hepatocytes via bile duct. The cited art teaches given its central role in metabolism and the production of serum proteins mammalian liver is an important target tissue for gene therapy using various viral and non-viral vectors (col.1, lines 40-67) The cited art further teaches the delivery of polynucleotide sequences into hepatic artery and portal vein (col.14 table-8, col.19). The cited art further teaches that in liver the parenchymal cells include hepatocytes, Kupffer cells and the epithelial cells that line the biliary tract and bile ductules (col.4, lines 33-49). The cited art further teaches that administration of polynucleotide sequences to bile duct wherein the permeability has been increased allow the transduction of hepatocytes in liver (col. 22, lines 18-31).

Thus it would have been obvious to modify the invention of Stedman who teaches transvascular delivery of a viral vector in a mammal by substituting the intra arterial or intravenous routes of administration with intra bile duct administration as taught by Wolff. One would have been motivated to do so to transduced liver cells that lines the biliary tract and/or bile ductules. One would have a reasonable expectation of success because the transduction of liver cells in-vivo has been routine in the art at the instant invention was made. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

### ***Claim Objections***

Claim 4 is objected to because of the following informalities: The instant claim recites claim limitation "recombinant virus" which does not further limits the viral vectors recited in this claim. Appropriate correction is required.

**Conclusion**


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Sumesh Kaushal  
Examiner GAU 1636

  
SUMESH KAUSHAL  
PATENT EXAMINER